Bedside Pulmonary Imaging to Guide Mechanical Ventilation: Dream or Reality?

John H. Arnold, M.D.
Children’s Hospital
Harvard Medical School
Boston, MA
Pediatric patient with ARDS: Computed Tomography
ARDS
CT and PV Curve (slow inflation)

M. Amato 2000 (personal communication)
Lung Recruitment

- Recruitment occurs throughout inflation
- Recruitment progresses from non-dependent to dependent lung
- Slow inflation to total lung capacity may not produce full recruitment
- Assessment of mean lung behavior does not allow effective lung protection
Ideal Clinical Monitor

- Non-invasive
- Portability to the bedside
- Short processing time
- Dynamic data updating
- Describes regional changes in anatomy/physiology
Production of a cross-sectional image of electrical impedance distribution in order to estimate air distribution
Electrical Impedance Tomography (EIT)

Resistivity (at 50 KHz) relative to blood:

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Relative Resistivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>whole blood</td>
<td>1</td>
</tr>
<tr>
<td>muscle</td>
<td>1.6</td>
</tr>
<tr>
<td>liver</td>
<td>5</td>
</tr>
<tr>
<td>lung, deflated</td>
<td>8</td>
</tr>
<tr>
<td>lung, inflated</td>
<td>16</td>
</tr>
<tr>
<td>bone</td>
<td>50</td>
</tr>
</tbody>
</table>
3 m/o, Bronchiolitis
Servo 300, PC/PS PIP 27, PS 10, PEEP 5

- Vt 35 cc
- Vt 25 cc
Regional ventilation in dependent areas
Regional ventilation in nondependent areas
Comparison of Two Strategies for Alveolar Recruitment in Children with Acute Lung Injury

John Arnold, MD
John Kheir, MD
Gerhard Wolf, MD
Brian Walsh, RRT-NPS, RPFT, FAARC
John Thompson, RRT
CHB Study

- n = 20 patients
- ARDS within 72 hours of intubation
- Comparison of two lung recruitment maneuvers
  - Sustained inflation
  - Maximal recruitment strategy
- End-points
  - Gas exchange (PaO₂ + PaCO₂ > 400)
  - Lung volumes
  - EIT images
Protocol Schematic

Pressure-Volume Curve Determination

Phase A – Baseline Ventilation
10 minutes

Phase B – Open Lung Approach
10 minutes

Phase C – Maximal Recruitment
≤25 minutes

Phase D – PEEP Titration
~20 minutes

Phase E – Followup
1 hour

ONLY IF PaO2 + PaCO2 < 400 mm Hg AND plateau pressure < upper inflection point

ΔP = 15 cm H2O

Tv = 6 mL/kg

'P380'

Time (sequence of study)

Ventilatory Pressure (cm H2O)

Represents measurement of lung volumes by nitrogen washout and electrical impedance tomography, arterial blood gas, static compliance, alveolar dead space, EBC pH
Patient 1 – PaO2 + PaCO2

Pressure-Volume Curve Determination

Phase A – Baseline Ventilation
10 minutes

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Phase E – Followup
1 hour

VENTILATORY PRESSURE (cm H2O)

0
10
20
30
40
50
60

Time (sequence of study)

Ventilatory Pressure (cm H2O)

Sustained Inflation

PC

Pflex + 2

VC

112

122

109

102

130

453

35

30

25

20

Pflex

PC

PC

PC

Pressure

ΔP = 15 cm H2O

ONLY IF PaO2 + PaCO2 < 400 mm Hg AND plateau pressure < upper inflection point

Tv = 6 mL/kg

End

'P380'

14

16

1 hour

5 mins

Represents measurement of lung volumes by nitrogen washout and electrical impedance tomography, arterial blood gas, static compliance, alveolar dead space, EBC pH
Ramping Plateau Pressure Recruitment

Plat 30 cmH$_2$O
Plat 35 cmH$_2$O
Plat 40 cmH$_2$O
Plat 45 cmH$_2$O

Back to VC – 6 mL/Kg
PEEP $\downarrow$ to 20 cmH$_2$O
Conclusions

- More atelectasis reversal in responders compared to non-responders
- Resolution of regional atelectasis precedes improvement in oxygenation (responders)
- Absence of atelectasis reversal predicts non-responders
- Overdistension precedes atelectasis reversal in dependent areas in responders
EIT Guided Ventilation in Experimental Acute Lung Injury

- Saline lavage-induced lung injury w/ injury augmentation
- Six hours of conventional ventilation
- Control group: ARDS Network ventilator algorithms
EIT Guided Ventilation in Experimental Acute Lung Injury

- EIT-guided group (regional EIT derived compliance calculation):
  1. PEEP increased (5 cm) to reverse atelectasis in dependent lung. When dependent compliance stops increasing,
  2. PEEP reduced (2 cm) to limit overdistension in non-dependent lung. When dependent compliance decreases,
  3. Maintain current PEEP and return to step 1 if dependent compliance decreases by more than 20% of its maximum value.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Whole Lung (24 samples per group)</th>
<th>Ventral Area (12 samples per group)</th>
<th>Dorsal Area (12 samples per group)</th>
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<tbody>
<tr>
<td></td>
<td>EIT</td>
<td>Control</td>
<td>EIT</td>
</tr>
<tr>
<td>GR</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>AB</td>
<td>1 (0-2)</td>
<td>1 (1-3)</td>
<td>2 (0-3)</td>
</tr>
<tr>
<td>IH</td>
<td>1 (0-2)</td>
<td>1 (0-3)</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td>ASE</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>HM</td>
<td>10 (42%)*</td>
<td>16 (67%)</td>
<td>9 (75%)</td>
</tr>
<tr>
<td>AF</td>
<td>18 (75%)*</td>
<td>24 (100%)</td>
<td>9 (75%)</td>
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GR = granulocytes; AB = intra-alveolar blood; IH = interstitial hemorrhage; ASE = alveolar septal expansion; HM = hyaline membrane; AF = airway fibrin. Data are median score (range) or number (%) for presence/absence of HM or AF. * denotes P < 0.01 according to repeated measures ANOVA.
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<td>Granulocytes</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>Alveolar blood</td>
<td>1 (0-2)</td>
<td>1 (1-3)</td>
<td>2 (0-3)</td>
</tr>
<tr>
<td>Interstitial hemorrhage</td>
<td>1 (0-2)</td>
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<td>1 (1-2)</td>
</tr>
<tr>
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<td>2 (1-3)</td>
<td>2 (1-3)</td>
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<td>Hyaline membrane</td>
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EIT = electrical impedance tomography.
*p < 0.01 according to repeated-measures analysis of variance.
Data are median score (range) or number (%) for presence/absence of hyaline membrane or airway fibrin.
The EIT Dream for Guiding Mechanical Ventilation
Future of EIT Guidance

Gas exchange stopping criteria

EIT stopping criteria

Paw
“I have yet to see a problem, however complicated, that when you look at it the right way does not become more complicated.”

--Paul Aldeston
A BENCH EVALUATION OF NITRIC OXIDE DELIVERY WITH THE PERCUSSIONAIRE VDR

Benitez, Christopher J BSRT, RRT; Crezeé, Kevin BS, RRT-NPS

1Respiratory Care Services, Primary Children’s Hospital, Salt Lake City, Utah

Abstract

Background: Primary Children’s Hospital (PCH) purchased and began using VDR ventilators in April of 2012. Previous to this time, PCH had used Sinusoidal Bronchotron (Percussionaire Sandpoint, Idaho) for all HFPV and HFNCAPAP ventilation. During this time, many discussions occurred regarding the best method for achieving appropriate Nitric Oxide delivery. This subject has been discussed and various recommendations from users at different facilities have been expressed. Ikaria has not been able to validate a method for injection or sampling of Nitric Oxide. Previous studies presented at Snowbird Conference in 2010 showed that a flow of 14 lpm introduced into the patient interface was required to achieve an analyzed concentration equal to the set concentration of INO with the Sinusoidal Bronchotron.

Method: The Percussionaire VDR 4 (Sandpoint, ID) was set up as a ventilator. Two types of Phasitron model were used. The now discontinued Turbohub Phasitron/RT 235 Neonatal Circuit (Fisher/Paykel Auckland NZ) combination, and the disposable Universal Phasitron at the airway circuit with a RT 240 Adult Circuit (Fisher/Paykel Auckland NZ). The VDR ventilator settings were verified on the VDR Monitor. VDR settings were maintained throughout testing at a Peak Pressure 35, Peep/CPAP 10, Convective Rate 20, Convective I:E ratio 1:2.0, I-time 1.0 seconds, E-time 2.0 seconds, Percussive rate 600, High Frequency I:E ratio 1:1.0. For the Turbohub testing, the injector module was placed at the gas outlet on the inspiratory side of the Turbohub. Flow rates were varied starting at 0, and then adjusted between 6 to 14 liters of blended gas injected into the fail safe valve on the inspiratory side of the turbo hub. Measurements are reported on flow of 6 to 14 liters when a change in measured NO was noted. The Universal Phasitron was tested with the injector module in two positions. First location was placing the injector module on the side of the humidifier that would be considered the dry side (directional into the humidifier chamber). The Nebulizer flow was turned on according to manufacturer direction. The second location was by adapting the white “Phasitron” driving line to place an injector module using 2.5 ETT tube adapters between the VDR and the Phasitron. Measurements were taken at the Phasitron outlet and also at the Neonatal circuit outlet connected to a test lung. The test lung was a Smart Lung Infant (IMT Medical Switzerland). The lung was connected to a 3.5 ETT and set for a resistance of 5 and a lung compliance of 2 ml/cmh2O. The INO device was an INO-Max DS, (Ikaria, Hampton NJ). The INO was set to deliver a 20 PPM dose. All devices passed manufacturer recommended pre-use / pre-calibration checks.

Results: The universal setup with the injector placed in the neb flow performed the worst with a delivered NO value of 1.3 ppm. The Universal setup with the injector in the white line provided a delivered NO value of 8.5 ppm. The Turbohub with no additional flow provided a delivered NO value of 42 ppm. For the Turbohub when flow was added at 6lpm delivered 27 ppm, 7lpm delivered 24 PPM, 10lpm delivered 23 ppm, 14lpm delivered 21 ppm.

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<th>Nitric Oxide Deliver with the VDR</th>
<th>NO2</th>
<th>% NO delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phasitron Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Universal - Neb flow</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>7%</td>
</tr>
<tr>
<td>Universal - White line</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>8.5</td>
<td>43%</td>
</tr>
<tr>
<td>Turbo Hub Phasitron</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>210%</td>
</tr>
<tr>
<td>Turbo Hub Phasitron</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>135%</td>
</tr>
<tr>
<td>Turbo Hub Phasitron</td>
<td>7</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>120%</td>
</tr>
<tr>
<td>Turbo Hub Phasitron</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>115%</td>
</tr>
<tr>
<td>Turbo Hub Phasitron</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>105%</td>
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Conclusion: Current methods of NO delivery with the Universal circuit setup do not achieve 50% of set versus measured dose with both placement locations of the Injector module and cannot be recommended for safe and effective delivery of INO. The Turbo hub setup with a flow of 7 lpm applied to the failsafe valve on the inspiratory side of the Turbo hub was required to achieve the 20% tolerance of set versus measured. Higher flows achieved a closer set versus measured NO concentration but doubling the flow decreased this from 24 to 21 PPM. With these added flows, there are potential effects of increased pressures. If nitric is added, adjustments may need to be made to the VDR settings to maintain set pressures.

Discussion: There are potential reasons for each of the failures of the two Universal setups. In the first setup, the injector module was placed on the humidifier with the 24 LPM of neb flow driving through the injector for humidification. This would require a certain amount of entrained gas from the inspiratory side of the Phasitron. In this model, the entrained gas rate was not high enough to significantly increase the delivered NO to the patient. The NO saturated gas was likely escaping from the expiratory side or entrainment gate valve. In the second universal setup with the injector on the white line between the VDR and the Phasitron, the flows through the white line are lower than the total flow. In this case, the opposite of the first test was happening. The entrainment flows were decreasing the overall concentration of INO in the circuit. Most likely the higher PPM during the second universal setup reading was due to the direct flow nature of the white line versus the entrainment and mixing in the first universal setup reading. In both cases, measurement accuracy will always be a question. The need to analyze gas drawn from an inspiratory fresh gas source is problematic, unless a Phasitron is used that minimizes mixing of inspiratory/expiratory gas. The Phasitron would have a mixed gas source for analyzed gas. Therefore, potentially higher overall pulsed concentration with each Phasitron pulse cannot be ruled out when the gas sampled is a mixed inspiratory/expiratory source.

Reference:
A Bench Evaluation of Nitric Oxide Delivery with the Percussionaire VDR

Christopher Benitez BSRT-RRT

Kevin Crezeé BS RRT-NPS
Disclosure Slide

• I have no relevant financial interests in today’s presentation

• All of the Nitric Oxide setups being discussed are currently not approved by Percussionaire or Ikaria. View expressed are from our experience and studies.

• Kevin Crezee
  – Clinical consultant with Ikaria (In-services, Tech Support, RT Advisory boards)
  – Clinical consultant with Discover Labs – RT Advisory boards
WALLY, DO YOU HAVE A MINUTE?

NOPE. I'M FAR TOO BUSY.

I'M BLOCKING THE ONLY EXIT. YOU HAVE NO CHOICE BUT TO ANSWER MY QUESTION.

I BLOCKED THE AIR VENT TOO.

WELL PLAYED.
Introduction

- Nitric Oxide Delivery/Gas Analysis is complicated by the Phasitron employed by the Percussionaire VDR
  - This is due to several factors
    - mixed inspiratory/expiratory gas at the Phasitron outlet.
    - Dual Gas Sources for breaths
- Ikaria recommends using injector module only for delivery due to safety features built into system with injector module
  - Suggested tolerance is 20% of set dose
Current Methods for Delivering INO

• Universal Setup with Injector Module
  – INO connected to dry side of humidifier from nebulizer flow
  – Cutting of driving line and placing injector inline

• Universal Setup Without Injector Module
  – Connecting additional flow to Phasitron at patient connection via blender setup on DSIR Setup
    • PPM is adjusted until desired PPM concentration reached
Current Method Using Turbohub Phasitron

- Placement of Injector module is the outlet of the inspiratory side of the Turbohub
- Flow added to fail safe valve on inspiratory side for testing purpose
Universal Circuit Setups Tested

- Tested only setups that used the injector module
  1. Injector module attached to dry side of humidifier driven by nebulizer flow
  2. Injector placed inline with white drive line
“So are you from out of state?”
Setting and Testing Method

• VDR Settings
  – Peak pressure 35
  – Peep 10
  – Convective rate 20, IE 1:2.0, I-time 1.0 Sec, E-time 2.0 Sec
  – High Frequency Rate 600 i:e 1:1

• Universal Phasitron NO delivered measurement done post Phasitron outlet to patient

• Turbohub NO delivered measurement post RT-235 circuit wye.
<table>
<thead>
<tr>
<th>Phasitron Type</th>
<th>Additional flow</th>
<th>Set NO</th>
<th>Measured NO</th>
<th>NO₂</th>
<th>% NO delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Universal - Neb flow</td>
<td>24</td>
<td>20</td>
<td>1.3</td>
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Conclusions

• The Universal circuit in both positions provided the lowest nitric dose.
  – This is most likely due to the mixing factor of the gas

• Turbohub
  – Over delivered Nitric by 200% + with no added flow
  – Best balance of 20% tolerance with flow of 7 added to the circuit
Discussion Points Delivery

- Injector on Humidifier Universal Circuit
- Due to low flows and small lung model minimal entrainment occurred
- Excess escapes out waste gate
Discussion Points Delivery Failures

- Injector in Delivery Line Universal Circuit
- Higher INO Number
- NO was diluted even with minimal entrainment
- Gas mixing and losses via exhalation
Turbohub Delivery Considerations

- Without added flow excessive delivery occurred
  - Hypothesized theory is that injector module double counts the flow in some manner
- Flow of 14 provided closest set to analyzed performance
  - Possible increases in Mean and Peep with added flow
- PCH utilizes a flow of 6 but will investigate increasing to flow of 7
Other Points to Consider

- Test done only with neonatal lung model
  - Larger patients may have a higher amount of entrainment and therefore higher

- Turbohub is no longer being produced
  - Renders safer method for delivery INO with Injector module unavailable
Summary

• There currently is no best practice established in literature

• Testing shows that an over delivery of Nitric would be required to achieve goal PPM with Universal Circuit

• Turbohub provided best delivery option with added flow but may change Peep and Mean characteristics of Ventilator
Would a fly without wings be called a walk?
A BENCH EVALUATION OF NITRIC OXIDE DELIVERY WITH THE PERCUSSIONAIRE VDR

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Reference:
Doing the Good You Were Called to Do.
A Celebration of What I Learned from Robert A. deLemos

Reese Clark FAAP
Conflicts/FDA

• I have no conflicts of interested related to the talk.
• I am not discussing use of any drugs – so no FDA disclosure.
My Time Line

• 1974 Finished High School
• 1974-1982 University of North Carolina Undergraduate and Medical School
• 1982-1987 Residency and Fellowship Training Wilford Hall USAF Medical Center in San Antonio, Texas
• 1987-1990 Attending at WHMC
• 1991-1997 Emory University
• 1997-1998 Duke University
• 1998 to present Pediatrix Medical Group
Robert DeLemos
Lesson 1 – Do what you are good at doing.

Pick a priority and complete the task before you move to the next project.
Early Years

• At Amherst he was a Bond Fifteen history major who became premed only in junior year.
• After Amherst he received his MD *cum laude from Harvard Medical School* in 1962
• He did an internship and residency at Children’s Hospital in Boston and his neonatal fellowship in neonatology at Johns Hopkins Medical Center.
• At Hopkins he worked with Mary Ellen Avery
• She came to visit WHMC to celebrate the work Dr deLemos was doing
The Event that Started Dr. deLemos on a Research Path

- Patrick Bouvier Kennedy had not been premature, he would have been born at Washington's Walter Reed Hospital.
- Just in case, the Air Force had long since readied a ten-room suite (nursery, kitchen, two lounges and six bedrooms) at Otis.
- On Aug. 7, 1963, the news from Otis Air Force Base on Cape Cod, Mass., flashed around the world: President John F. Kennedy and his wife, Jacqueline, had welcomed a third child.
- The boy arrived at 34.5 weeks and weighed 4 pounds, 10.5 ounces.
- Patrick Bouvier Kennedy newborn suffered from hyaline membrane disease, a lung ailment that at the time was the No. 1 killer of babies born before full term.
- Rushed from Cape Cod to one of the finest hospitals in the world: Children’s Medical Center in Boston.
A Kennedy Baby’s Life and Death, NY times
By LAWRENCE K. ALTMAN, M.D.
Published: July 29, 2013
In 1963, medicine had little to offer babies with the HMD, other than warm incubators and good nursing care.

If a baby made it through on its own for 48 hours, its chances of survival were good.

There were very few NICUs in 1963, just a few good pediatricians who were trying to develop NICU services.

Moreover, it was August, and most of the senior physicians were on vacation, recalled Welton M. Gersony, then training in pediatric cardiology.

“The junior doctors felt overwhelmed and were desperate to get a senior person,” said Dr. Gersony
In an effort to save the child, doctors placed him in a steel hyperbaric chamber 31 feet long and 8 feet in diameter to force oxygen into his lungs.

Patrick’s tiny heart gave out, and he died just 39 hours after birth.
What Dr. DeLemos taught us as Resident and Neonatal Fellow
Work Done as a Resident and Fellow


• Oxygen is a toxic drug
• Steroids play a role in surfactant metabolism
What Dr. DeLemos taught us as an USAF officer and Junior Faculty Member
Early Neonatal Research at Wilford Hall US Air Force Medical Center
Donald M. Null, Bradley A. Yoder and Robert J. DiGeronimo
*Pediatrics* 2012;129;S20
DOI: 10.1542/peds.2010-3797e

• The beginning of the many contributions to the field of neonatology originating from Wilford Hall Air Force Medical Center began when Robert deLemos, MD was assigned to Lackland Air Force Base (AFB) in the summer of 1969.

• Dr. deLemos was the *first and only fully* trained Air Force neonatologist at a time when neonatal medicine was still just in its infancy.
Ventilation

The Bird Ventilator
THIS STARTED AS A VENTILATOR FOR HORSES
What is a Priority

• A priority is something (an object, value, goal, relationship, a cause) which is of leading importance in our life. We live for it and it gives focus and purpose to our life.

• A priority is a guiding value around which the rest of our life tends to be ordered, for better or worse.

• A priority is that part of our life and ideas that has first claim on our time, our thoughts, our energy, our resources, our money, and our happiness.

• If you spend your time, talent, money and thoughts on something which is not really a priority you will be unhappy.
Creating a Priority

• **Imagination:** Our imagination allows us to envision the possibilities and the alternatives. Our imagination allows us to dream dreams; to define ideals and to hope for a better life.

• **Intelligence:** Our ideas and brain work allows us to think through the course that lies ahead; to reason through complex challenges along the path, to evaluate all the possible interactions that may confound our choices and finally to plan a route to the next goal we have set to help us stay true to our priorities.

• **Will power/Discipline:** Our will allows us to resolve, to seek our desired goal. Our will gives us the grit to stick with a chosen course of action and not to abandon the course we have chosen. Applying our will prevents us from being bound by impulse or instinct, to transcend the givens of an inherited situation.


Example

• Think about the first medical paper you wrote.
  • How did you start
  • What were the key elements to getting it published
    • Imagination (deciding what to study)
    • Intelligences (stating an hypothesis and making a study plan)
    • Will/Resolve (doing the study)
    • Action (writing the paper and submitting it)
Are You or Others Choosing

• Are you just responding to the expectations of others, acting out of convenience, living to avoid certain circumstances or just melting into the cultural norms?

• Our priority is only authentic if we set it after careful reflection and consideration about the kind of life we want to live.

• “The world will ask you who you are and if you do not know, the world will tell you.” (Carl Jung)
What are your priorities?

• Are they written down?
• Who is your team and how will they help you accomplish your priorities?
• Is it balanced?
Competing priorities

- Family – wife/children/parents/pets
- Friends
- Work
- Spiritual health
- Physical health
Lesson 2

COLLABORATE DO NOT COMPETE WITH OTHER AWESOME SCIENTIST AND BE WILLING TO SHARE THE CREDIT
List is too long to record.
Here are just a few of the scientist that collaborated with or were trained by Dr. DeLemos

- Avery, M.E.
- Kirby, R.R
- Schulz, J.
- McLaughlin, G.W
- Null, D.M., Jr
- Stoddard, R.A.
- McCurnin, D.C.
- Ackerman, N.B.
- Bell, R.E.
- Meredith, K.S.
- Coalson, J.J.
- Walsh, W.F.
- Gilstrap, L.C., III
- Hauth, J.C.
- Yoder, B.A.
- Cornish, J.D
- Prihoda, T.J.
- Gerstmann, D.R.
- Winter, V.T.
- Kinsella, J.P.
- Morrow, W.R.
- Minoo, P.
- Segura, L.
- King, R.J.
- Taylor, A.F.
- Lally, K.P.
- Chwals, W.J.
- Dreyer, G.L.
- Snyder, G.E.
- Kuehl, T.J.
- Leach, C.L.
- Greenspan, J.S.
- Shaffer, T.H.;
- Wolfson, M.R.;
- Fuhrman, B.P.
- Tantivit, P.;
- Subramanian, N.;
- Garg, M.;
- Ramanathan, R.
- Maxwell, L.C.
MUCH OF WHAT WE KNOW ABOUT HOW BEST TO USE RESPIRATORY SUPPORT WE LEARNED AT WHMC AND IN THE BABOON LABORATORY

• In 1991, Kinsella et al reported the hemodynamic consequences during the first 24 h of life in premature baboons (140 d) with hyaline membrane disease that were treated with high-frequency oscillatory ventilation (HFOV) or conventional intermittent mandatory ventilation (IMV).

• Cardiac output and organ blood flow were measured at three time-points using the radiolabeled microsphere technique. By design, initial mean airway pressure (Paw) was higher in the HFOV group (p less than 0.01).

• There were no significant differences in left ventricular output, effective systemic flow, organ blood flow, or central venous pressure between the two groups at 3, 8, or 23 h.

• The HFOV strategy used in our study resulted in significant improvement in oxygenation during the initial 24 h of treatment without adverse effect on left ventricular output, cerebral blood flow, or central venous pressure.

• Kinsella et al concluded “that when appropriate changes in Paw are made during HFOV in response to improvement in arterial oxygenation and changes in lung inflation as assessed by chest radiographs HFOV can be achieved without depressing cardiovascular dynamics more than during conventional therapy with IMV”

• The conclusions of this study define how best to use HFOV in infants with respiratory distress syndrome and served as the model for all subsequent clinical trials comparing HFOV and conventional ventilation.
Open Lung Ventilation Strategy

Froese AB. High-frequency oscillatory ventilation for adult respiratory distress syndrome: let's get it right this time! Crit Care Med 1997; 25: 906-908.

$Pao_2$ (kPa)

![Graph showing $Pao_2$ over time with different ventilation methods.

$PPV_{OLC}$, squares; $HFOV_{OLC}$, circles; $PPV_{CON}$, triangles]

Sections of lungs stained with hematoxylin-eosin, magnification 50×. (A) Diffuse atelectasis, hyaline membrane formation, and cellular infiltration in the lung of an animal treated with PPVCON. (B) Increased cellular infiltration in the lung of an animal treated with PPVOLC. (C) Increased cellular infiltration in the lung of an animal treated with HFOVOLC. (D) Minimal signs of structural damage to the lung of an animal undergoing lavage only.
MUCH OF WHAT WE KNOW ABOUT BPD WAS THE RESULTS OF THE COLLABORATION BETWEEN DOCTORS COALSON AND DELEMOS


Coalson and deLemos Collaboration


OLD BPD

• Findings from lung specimens of 121 prematurely delivered baboons at 0, 0.5, 1, 2, 3–6, 7–11+ days after delivery document that the premature lung has a delayed and more blunted exudative response when compared to that of human and baboon adults.

• Saccular edema, not hyaline membranes, is the dominant histopathological finding in the exudative phase of diffuse alveolar damage and occurs later (7–11 days) in infant lungs when compared to comparably treated adult lungs in which maximal exudative changes are seen at 3–6 days.

• The reparative response in the premature baboon is characterized by saccular wall thickening and fibrosis, with less intramural organization of exudate in saccular/alveolar spaces when compared to adults.

• The airway changes in the premature are more severe than those seen in adult disease
Evolution of disease 6 hours to 48 hours

Fig. 3. A 6-h specimen. A hyaline membrane (HM) composed of protein coagulum and degenerated cellular organelles is adhered to denuded basement membranes at one site (double arrows) and then extends over edematous type I epithelium (arrow) and a type II cell (ATII) that is devoid of lamellar inclusion bodies. The sacculal space (AS) is filled with edema and the interstitium (I) contains many cellular elements. The endothelium of the capillary (C) appears normal. Lead citrate and uranyl acetate, ×2470.

Fig. 4. A 48-h 100% O₂-treated specimen. Endothelial damage is evident in the capillary (C). An intercellular junction (arrow) clearly delineates the marked difference in cytoplasmic osmiophilia. The interstitium (I) contains abundant cells and a few collagen fibers. Portions of three alveolar type II cells (ATII) are present. Lead citrate and uranyl acetate, ×3,120.
100% OXYGEN VS PRN OXYGEN


Fig. 11. A 17-day 100% O₂-treated specimen. The altered inflation pattern, seen consistently in the 7-11+ day specimens, is very exaggerated by 17 days. Sites of overinflation with "simplification" of the involved sacular walls alternates with atelectatic and/or fibrotic bands. B, bronchus; A, pulmonary artery. Hematoxylin and eosin, ×20.
Coalson JJ. Pathology of bronchopulmonary dysplasia. *Semin Perinatol* 2006; 30: 179-184..

- Over the past three decades, advances in prenatal and neonatal intensive care have contributed to marked improvements in survival rates for extremely immature infants.
- Infants born at 24 to 26 weeks are in the canalicular phase of lung development
- This is a time when alveolar and distal vascular development is rapidly occurring

- The histopathological lesions of severe airway injury and alternating sites of overinflation and fibrosis in "old" BPD have been replaced in "new" BPD.
- The change seen in the “new” BPD are:
  - large, simplified alveolar structures
  - a dysmorphic capillary configuration
  - variable interstitial cellularity and/or fibroproliferation
- Airway and vascular lesions, when present, tend to be present in infants, who over time develop more severe disease.
- The concept that "new" BPD results in an arrest in alveolization should be modified to that of an impairment in alveolization as evidence shows that short ventilatory times and/or the use of nCPAP allow continued alveolar formation.
Figure 2. The 33 wk PRN control and BPD survivors. The control specimen (A) displays numerous respiratory bronchioles, alveolar ducts, and alveoli, seen at higher magnification in B. Compare these micrographs to the BPD survivor micrographs in C and D. A subtle merging from normal appearing lung to lung with "enlarged airspaces" is seen in C, and a higher magnification of the enlarged airspaces is depicted in D. Many of the airspaces lack distinguishing features. Hematoxylin and eosin. Original magnifications: >50, >100, >500, >120.

Figure 4. Total internal surface area (TISA) of the BPD group is significantly decreased compared with the control group of PRN animals. This measurement clearly demonstrates that a lack of alveolarization was present in the BPD group.

Figure 5. Total alveolar counts differ significantly between the two study groups at 33 wk. Data are expressed as number of alveoli × 10^6 per lobe.
Figure 6. Volume density determinations are depicted. The volume of Type 2 cells is greater in the BPD group compared with that of the control group, and the Type 1 cell value is significantly increased in the control group compared with the BPD value.

Decreased alveolar septation in baboon survivors of BPD. Preterm baboons were delivered and randomized to ventilation with low or high supplemental oxygen for 21 days. The high oxygen plus ventilation-exposed group developed BPD. The BPD animals survived until 33 weeks of age, and biopsies of the lungs demonstrated larger distal airspaces than preterm ventilated animals exposed to less supplemental oxygen.

Cited by JOBE AH. The New BPD. NeoReviews 2006; 7: e531-e545.
DO YOU SEE A PATTERN

HYPOTHESIS

TEST

REPORT/TEACH
Lesson 3

TEACH OTHERS
He taught lots of folks

• Bob was the chairman of pediatrics at Wilford Hall Hospital at Lackland Air Force Base in San Antonio.
• After **retiring from the Air Force as a full colonel**, he was the chairman of the Department of Physiology and Research at the Southwest Foundation for Biomedical Research in San Antonio.
• He was a consultant to the Surgeon General of the U.S. Air Force. He helped decide where we all got assigned.
• In 1991 he moved to California and became Chief of Neonatology at the University of Southern California in Los Angeles, and Hastings Professor of Pediatrics and director of neonatal intensive care at Good Samaritan Hospital.
The People He Trained Continue to Contribute

- Neal Ackerman
- Richard Bell
- Cathy Bohanon
- Jan Carter
- Reese Clark
- Devn Cornish
- Dale Gerstman
- George Groberg
- Chip Howell
- Chris Johnson

- David Johnson
- Andy Kairalla
- John Kinsella
- Keith Meredith
- Stephen Minton
- Donald Null
- Gary Snyder
- Ron Stoddard
- Bill Walsh
- Brad Yoder
• He pushed us to be academically productive and not to be “academically lazy”
• He supported us through failed experiments, poor outcomes, and letters of rejection for publications.
• He carefully explained that adding to scientific knowledge is challenging
• He applauded our successes
• He loved debate and the passion of heated discussion
• He fostered in each of us a rugged independence and a propensity to challenge conventional wisdom
High-frequency nasal ventilation for 21 d maintains gas exchange with lower respiratory pressures and promotes alveolarization in preterm lambs


Affiliations | Corresponding author

Pediatric Research (2014) | doi:10.1038/pr.2013.254
Received 03 July 2013 | Accepted 26 September 2013
Accepted article preview online 30 December 2013 | Advance online publication 29 January 2014
Focus

• “...keep the main thing the main thing” (Stephen Covey)

• First things should be kept first – high important pursuits should not be interrupted by unimportant distractions.
Lesson 4 – Approach Life with Enthusiasm
Slow up early and often and help

• We all still have a lot to learn
• When Dr. deLemos showed up for morning rounds you were going to learn something
• And when he showed up at 4 am to look at xrays you best know what the xray showed
• Providing good care means always knowing everything you can know about your patient
• If your patient was sick you best be at his/her bed
Lesson 5

Promote innovation
ECMO

• In late 1984, Devin Cornish initiated steps to start an extracorporeal membrane oxygenation (ECMO) program.
• At this time, ECMO was considered largely an experimental therapy and was only being offered at a few centers within the United States.
• A story that very few people know even today is that in 1972 a neonate dying of respiratory failure was successfully placed on extracorporeal bypass with a membrane oxygenator in the NICU at Wilford Hall by Dr. deLemos.
• Dr Cornish, along with Drs Null and deLemos, established the military’s first and only ECMO program at Wilford Hall in 1985.
• Wilford Hall was the 12th center to open in the United States and the first to open in Texas and it was the only program west of the Mississippi River.


- A retrospective chart, literature, and database review of pediatric and neonatal patients transported on ECMO by the WHMC ECMO transport team November 1985 and September 2001.

- **Forty-two patients** transported on ECMO were identified: 23 neonatal respiratory cases (survival 57%), 7 pediatric respiratory cases (survival 71%), 4 cardiac cases (survival 50%), and 8 extra-institutional ECMO transports (survival 63%).

- In the MAS subpopulation, there was significantly greater survival in the in-house group--97% (31/32)--than in the ECMO transport group--75% (9/12)

- **No ECMO-related complications leading to patient demise were identified.**
Lt. Col. (Dr.) Dan Dirnberger, 59th Maternal/Child Care Squadron Neonatal Intensive Care director, and Maj. (Dr.) Melissa Tyree, Extracorporeal Membrane Oxygenation transport team director, provide care to a critically ill infant during the flight from Kadena Air Base, Japan, to San Antonio, MAY 2009.
Several updates of this experience have been additionally reported, with the most recent publication noting an average distance of 1380 miles per transport, including several transports from Okinawa, Japan, involving distances of >7500 miles.
Third Generation Cart
Lesson 5

Serve others
• Chris Plauché Johnson dream was to have a summer camp for children with special needs
• Founded in 1979, CAMP was incorporated as a 501(c)(3) nonprofit organization in 1980.
• In 1988 CAMP purchased a campground on the Guadalupe River in Center Point, Texas,
• Accredited by the American Camp Association in 1992.
• Dr. deLemos’s parents ran a camp in New York throughout his childhood.

• One of his passions was a camp for disabled children near San Antonio, called Children’s Association for Maximum Potential (CAMP).

• Dr. D (his CAMP name) was a founding board member and served as president for 17 years.

• He spent essentially much of his vacation time for many years at CAMP, even after he moved to Los Angeles.

• CAMP’s mission was to give kids with special needs a true camp experience
• The families of children who attend know their children are in a safe environment.
• Dr. D and Johnson ensured that even the most medically fragile child could get to CAMP. They developed an “ICU area” that would allow children undergoing home ventilation to experience CAMP.
• He later became the head cook in addition to being “Top Doc.”
• He sang with the children, helped them swim and canoe, and cried with joy at the end of camp when the parents viewed all the smiling pictures of their children playing in the hill country outside San Antonio, Texas.
Balance

• Once you have set your priorities and written them down your goals find balance.
  • Spirit
  • Family
  • Health
  • Productivity
  • Money

• This is the hardest task

• *Workaholics are far too common in medicine*
Lesson 6

Take a Stand
When California moved to cut off prenatal care to illegal immigrants, deLemos warned: "The dollars saved by excluding these women from programs that provide prenatal care will be offset thousands of times over by the medical costs of caring for their infants and the loss of tax revenues to the state."
Strengths

• What are your strengths?
• What makes you excited about work?
• "Make a living by doing what you enjoy, and you never have to work a day in your life."- Confucius
Most Important Lesson – Have Good Friends
Simple Truths that Are Commonly Forgotten

• Life is short and children grow up fast
• Happy memories make us smile when smiling is hard.
• They make the walk through tragedy bearable.
• Money does not create happiness. The love of money kills
• Work partners are like husbands/wives; they should be chosen with great care.
• Never and always are too certain. We can not see the future and miracles do happen.
• It is rarely too late to change career focus
• What ever you choose, pursue it with enthusiasm
• Showing up is more important than talking
• Please, thank-you, sorry, forgive me and love you are very important words